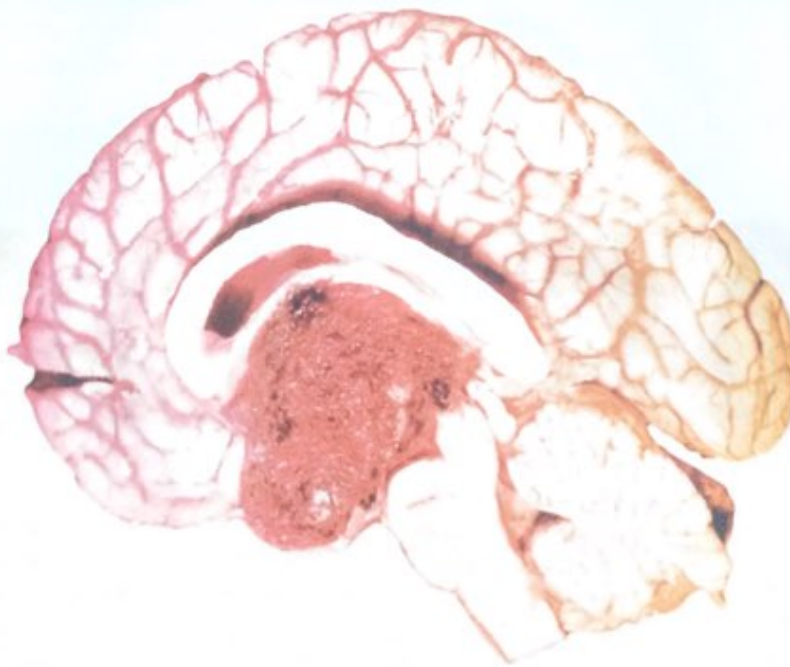


Easy Pathology

— Dr. Abdelrahman Khalifa —

CNS & Peripheral Nerves



Ain Shams 2017 - 2018

VISIT...

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CNS Tumors

• 1ry



- Meningioma & meningiosarcoma
- Gliomas (Astrocytoma – Oligodendroglioma – Ependymoma)
- Neuronal (neuroblastoma – Ganglioneuroma-Ganglioneuroblastoma)
- Nerve sheath (Schwannoma – Neurofibroma) → in peripheral nerves
- Vascular (hemangioma)
- Pineal body tumors
- Choroid plexus adenoma & carcinoma
- Embryonic (Medulloblastoma) → from cerebellum
- Malformative mass (craniopharyngioma- Cystic lesions 'dermoid, epidermoid, Colloid') → epidermal secretion

• 2ry (metastatic) e.g. Melanoma Menegial deposits e.g. Leukemia

• Lymphoma

Meningioma

Sites: external – Internal (ventricular)

Gross: rounded well defined – capsulated- whorly – grayish white - Firm

Micro:

Benign (WHO grade I):

-Syncytial: with whorly pattern. Indistinct borders.

-Fibroblastic: similar to fibroblasts + Collagen

-Transitional (Mixed)

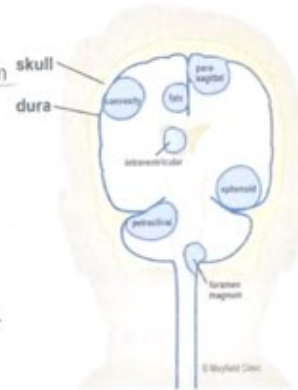
-Psammomatus: excess psammoma bodies calcification

Atypical locally malignant (WHO grade II): frequent abnormal mitoses.

Anaplastic malignant (WHO grade III): Sarcomatoid & invasion

Prognosis depends on Size, location, and grade

Complications: Benign → compression, Atypical & anaplastic → infiltrative & destructive

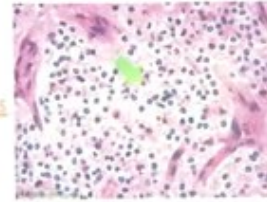


Astrocytoma (80% of adult 1ry tumors)

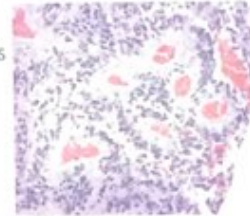
Grade I Piloicytic	Grade II Diffuse Fibrillary	Grade III Anaplastic	Grade IV Glioblastoma
Children Cerebellar	Children & adults Cerebellar or brain	Adults Brain	Adults Brain
Rounded mass Cystic or solid	Ill defined Grayish white	Irregular ill defined Grayish white	Irregular ill defined Grayish white areas Yellow necrotic areas Red hemorrhagic areas
Few bipolar cells with hair-like processes Rosenthal fibers & granular bodies	Hypercellular & fibrillary background Nuclear atypia	+ mitosis	+ N/H Vascular proliferation pallisading
Benign	Benign	Border line	Malignant

Oligodendroglioma:

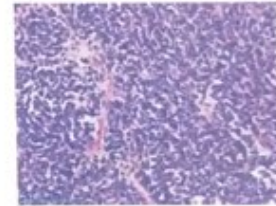
- Solid or cystic, with calcification
 - **WHO grade II**: Rounded cells with clear halo around nucleus + calcifications *أصباح*
 - **WHO grade III**: Anaplastic with frequent mitoses
- prognosis is **better** than astrocytoma

Ependymoma:

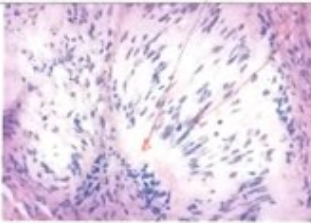
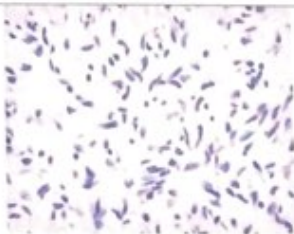
- From ependymal cells (lining of ventricles & spinal canal). Solid or papillary mass
- Cells are arranged in rosettes or perivascular pseudorosettes
- in children → Hydrocephalus, recurrent. In adults → compress spinal cord
- **WHO Grade II or III** (anaplastic)

Medulloblastoma (20% of brain tumors in children)

- Originating from cerebellum and invading medulla
- Children less than 6 years (embryonic)
- irregular ill defined mass with N/H
- Highly cellular small malignant blue cells with Anaplasia forming rosettes
- Highly malignant (Grade IV). But radiosensitive.



*undifferentiated
cells*

Schwannoma	Neurofibroma
<i>may difficult to distinguish</i> Cranial nerve <u>VIII</u> No skin patches	<u>Sensory</u> nerves (subcutaneous nodules) <i>بقعة بيضاء</i> <u>café au lait</u> skin patches in case of <i>بقعة بيضاء</i> neurofibromatosis
<u>Capsulated</u>	Not capsulated
Elongated cells with <u>pallisading of neuclei</u> (<u>Antoni A</u>) myxoid stroma (<u>Antoni B</u>)	Spindle cells collagen stroma
	
<u>Benign</u>	<u>Benign</u> → Malignant nerve sheath tumor

Complications of I.C. tumors:

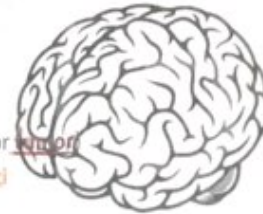
Compression & edema – Hemorrhage – Hydrocephalus- Herniation of brain *from foramen magnum*
- hemiparesis

Crebral edema

excess fluid in brain **parenchyma**

intracellular

- **I.C.** (**degeneration** due to cerebral injury)
- **E.C.** (increased vascular permeability due to **inflammation** or **trauma**)
brain is enlarged, **Soft**, **thick gyri**, **narrow sulci**



Hydrocephalus

excess CSF fluid in **Ventricular** system

بالدورة **Communicating:** excess **production** (**choroid tumor**) – decreased **absorption** (1ry **arachnoid defect**)

Non communication: Obstruction by **mass** or **tumor**

Effects: Head enlargement - Compression



Acute Meningitis

Inflammation of **Leptomeninges** with CSF in subarachnoid space

	Septic (Pyogenic)	Aseptic (viral)
Aetiology	Menengiococci (Adults) Pneumococci (Children) E-coli, Beta Strept (in Neonates)	Enteroviruses Measles, mumps, Influenza
Morphology	Pus & fibrin in subarachnoid space dilated vessels	Lymphocytic infiltrate
✓ CSF changes	excess amount excess neutrophils & bacteria excess proteins reduced glucose → <i>hypoglycemia</i> <i>confused by bacteria</i> <i>d.t. vomiting</i>	excess amount excess Lymphocytes moderate proteins Normal glucose
Complications	Spread: Encephalitis, pyemia & septicemia <i>by toxins</i> → Adrenal necrosis (Waterhouse Friedrichsen) Fibrosis → cranial nerve compression - Hydrocephalus	Usually Self-limiting

Chronic meningitis:

TB: CSF excess mononuclear cells, protein & normal glucose + **Tuberculoma**

Syphilis:

Meniovascular: Gumma → vascular narrowing → cerebral ischemia

Tabes dorsalis: degeneration of posterior column

مشلول و جنون **GPI** Generalized paralysis of **Insane** *يعجز البع*

Brain Abscess

spread from vertebral venous plexus
Aetiology: Pyogenic bacterial
 direct from (sinusitis) → frontal Otitis media → temporal pyemia → multiple abscesses meningitis
Morphology:

- Irregular cavitation (liquefaction) – surrounding brain is edematous
- **Microscopic:** liquefied tissue + neutrophils
 wall of acute abscess is necrotic – wall of chronic abscess is smooth 'gliosis'

Complications: Pressure → effects According to site (could be fatal) , Spread

MCQ Infections

animal bite *to CNS*
Rabies: Viral infection affecting nerve cells . cytoplasmic inclusions negri bodies
 Fate: muscle paralysis , respiratory failure → *respiratory failure & paralysis of respiratory muscles*



by ingestion **Poliomyelitis:** Viral infection of AHC → degeneration & necrosis → Limb paralysis

Fungal encephalitis: Candida, mucormycosis, Aspergillosis → Suppurative granuloma

Effects of HIV: Meningitis (Opportunistic infections) – AIDS dementia - Tumors → *على مستوى المخ واورام*

Demylinating & degenerative diseases

تصلب الجذع **Multiple sclerosis:** Autoimmune demylinating disease with attacks of neurological deficits genetic or viral factors. Common in females 20-40 y.

Morphology: demylinated nerve (myline -ve) . Preserved nerve axon (Silver stain)
Comp. / Resp. failure

Alzheimer's: Dementia of Old age > 50y *degenerative*

Morphology: Amyloidosis of cerebral vessels → brain atrophy + Cytoplasmic filaments

microscopic *atrophy of gyri + widening of sulci*

Parkinsons: Idiopathic tremors in old age (Inherited) → decreased synaptic transmission

Morphology: Intracellular inclusions (Lewy body)



Peripheral Neuropathy: demylination of peripheral nerves → decreased conduction

1-Diabetic neuropathy : sensory polyneuropathy → numbness *تخدير*

2-Inflammatory (e.g. SLE) : segmental neuropathy

3-Guillain-Barre: viral infection → Immune reaction → motor neuropathy (fatal)

Same as multiple sclerosis

Resp. failure

Cerebrovascular diseases

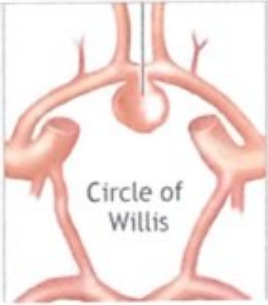
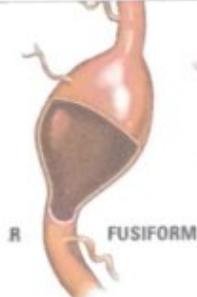
Transient ischemic attack	Stroke
Sudden cerebral neurological symptoms disappear before 24 hours	Sudden cerebral neurological symptoms last > 24 hours

Cerebral infarction:

Thrombosis, emboli, atherosclerosis → Liquifactive necrosis (more common in basal ganglia) → heal by gliosis



Cerebral aneurism

Congenital (Berry)	Mycotic	Atherosclerotic
Circle of Willis	Branches of middle cerebral	Internal carotid & basilar A.
Congenital defect of collagen & internal elastic lamina	Infection of the wall <i>by SBE, septic emboli, inf.</i>	Atherosclerosis
Multiple Saccular	Mushroom-shaped <i>fungus-like</i>	Fusiform
		
Associated with <u>polycystic kidney</u> <i>congenital</i>	Associated with <u>SBE</u> , or <u>PAN</u> <i>septic emboli, inf., vasculitis → necrosis of wall</i>	--

Complications: Compression – Rupture – Thrombosis & calcification

Vascular malformations:

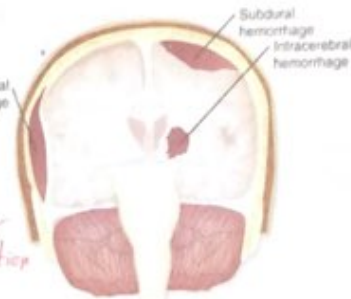
- Arteriovenous malformation: mass of arteries & veins → subarachnoid hemorrhage
- Cavernous Hemangioma: Large vessels separated by fibrous septa
- Capillary telangiectasia: dilated capillaries separated by brain tissue

dilated capillary



Intracranial hemorrhage

- ① Extradural: (epidural) trauma of middle meningeal artery → fatal
 - ② Subdural: Trauma of cortical veins → apical
 - ③ Subarachnoid: causes ruptured aneurism or ruptured vascular malformation
 - Traumatic
 - Spontaneous: mostly basal ganglia
- Hypertension (arteriosclerosis & microaneurisms) – Aneurisms – Blood diseases – Tumors
- Petechial spots - or extensive



Leads to: Hemiplegia – Compression – Herniation

- ④ *Intracerebral causes/HTN & blood diseases + tumors (bleeding tendency)

1. A 70 years old male complaining of headache and vomiting. Radiologic examination revealed multiple space occupying lesions in the temporal lobe of the brain. Biopsy taken from one of these lesions showed sheets of malignant cells which are large with small central nuclei and abundant granular eosinophilic cytoplasm. The most possible diagnosis:

- a) Anaplastic astrocytoma
- b) Glioblastoma multiforme
- c) Metastatic bronchogenic carcinoma
- d) Metastatic renal cell carcinoma
- e) Metastatic colonic adenocarcinoma

2. The following malignancy sends metastasis mainly to meninges:

- a) Breast carcinoma
- b) Bronchogenic carcinoma
- c) Renal cell carcinoma
- d) Acute leukaemia
- e) Laryngeal carcinoma

3. A patient with multiple skin nodules and skin hyperpigmentation, biopsy from the nodules shows a benign connective tissue neoplasm.

The most possible diagnosis is:

- a) Lipomatosis
- b) Neurofibromatosis
- c) Neurofibroma
- d) Schwannoma
- e) None of the above

4. Pilocytic astrocytoma is characterized by all Except:

- a) Usually occur in children
- b) Usually occur in cerebellum
- c) It is usually cystic
- d) It is of bad prognosis

5. The cause of death in rabies is:

- a) Muscle paralysis
- b) Heart failure
- c) Paralysis of respiratory muscles
- d) Respiratory center failure
- e) Septicemia

6. Astrocytoma is:

- a) Glial tumor
- b) Neuronal tumor
- c) Tumor of undifferentiated cells
- d) Nerve sheath tumor
- e) Malformative tumor

7. Subarachnoid haemorrhage is due to :

- a) Trauma of meningeal artery
- b) Trauma of cortical veins
- c) Rupture of cerebral aneurysm
- d) Sudden rise of blood pressure
- e) Haemorrhagic blood disease

8. Alzheimer's disease is :

- a) Congenital disease
- b) Inflammatory disease
- c) Degenerative disease
- d) Demyelinating disease
- e) Metabolic disease

9. Oligodendroglioma is not a :

- a) Glial tumor
- b) Cerebral tumor
- c) High grade tumor
- d) Well circumscribed tumor

10. The tumor which is formed of two growth patterns (Antoni A and B) is:

- a) Astrocytoma
- b) Oligodendroglioma
- c) Medulloblastoma
- d) Schwannoma
- e) Ependymoma

11. Psammoma bodies are characteristic of:

- a) Astrocytoma
- b) Oligodendroglioma
- c) Medulloblastoma
- d) Meningioma
- e) Schwannoma

12. A previously healthy 31-year-old woman experiences extensive subarachnoid hemorrhage at the base of the brain. She is afebrile. The CSF protein is slightly increased, but the glucose is normal. Which of the following is the most likely diagnosis?

- a) Acute bacterial meningitis
- b) Ruptured berry aneurysm
- c) Cerebellopontine angle tumor
- d) Pilocytic astrocytoma
- e) Meningioma

13. A 50-year-old man has a 3cm diameter left frontal lobe mass with areas of calcification. Microscopically, sheets of regular cells with spherical nuclei surrounded by clear halo of cytoplasm are seen. Which of the following diagnosis is most likely to be made on microscopic examination of this mass?

- a) Thrombosed berry aneurysm
- b) Oligodendroglioma
- c) Meningioma
- d) Schwannoma
- e) Organizing abscess

14. A 9-year-old child has enlargement of the lateral ventricles with a 4 cm homogenous, well-circumscribed mass within the fourth ventricle. Which of the following is the most likely diagnosis?

- a) Astrocytoma
- b) Ependymoma
- c) Meningioma
- d) Metastatic carcinoma
- e) Schwannoma

15. A 65-year-old man develops new-onset seizures and headaches. A CT scan reveals a 6 cm left-sided intracerebral mass. Which of the following is the most likely diagnosis?

- a) Meningioma
- b) Metastatic testicular carcinoma
- c) Schwannoma
- d) Glioblastoma multiforme

16. A 10-year-old girl develops ataxia and hydrocephalus. CT scan shows a midline cerebellar mass. Which of the following is the most likely diagnosis?

- a) Astrocytoma
- b) Meningioma
- c) Neurofibroma
- d) Medulloblastoma

17. The biopsy of a ring-enhancing tumor in the left parietal lobe of a 60-year-old patient reveals an astrocytic tumor that displays marked cellular atypia, mitotic activity, areas of pseudopalisading necrosis and multifocal microvascular hyperplasia. The diagnosis is:

- a) Astrocytoma, grade 1
- b) Astrocytoma, grade 2
- c) Anaplastic astrocytoma
- d) Astrocytoma, grade 4 (glioblastoma multiforme)
- e) Pilocytic astrocytoma

18. Poliomyelitis is usually an infection of:

- a) Cerebral tissue
- b) Cerebellar tissue
- c) Anterior horn cells of spinal cord
- d) Posterior horn cells of spinal cord
- e) Peripheral nerves

19. Rabies is transmitted to CNS via:

- a) Arteries
- b) Veins
- c) Peripheral nerves
- d) Direct implantation
- e) Lymphatics

20. Infection spreads from suppurative lung disease to the brain via:

- a) Vertebral arteries
- b) Vertebral veins
- c) Local extension
- d) Peripheral nerves
- e) None of the above

21. Modes of infection in pyogenic meningitis include all EXCEPT:

- a) Blood spread
- b) Blood transfusion
- c) Local spread from paranasal sinuses
- d) Direct implantation in case of skull fracture

22. A five years old child suffered from headache and blurring of vision. Radiologic examination showed a cerebellar tumor. Microscopic examination of a biopsy specimen from this tumor revealed diffuse infiltration by malignant small round cells with rosette formation. The most possible diagnosis is:

- a) Anaplastic astrocytoma
- b) Glioblastoma multiforme
- c) Ependymoma
- d) Neuroblastoma
- e) Medulloblastoma

23. Medulloblastoma is:

- a) Glial tumor
- b) Neuronal tumor
- c) Tumor of undifferentiated cells
- d) Nerve sheath tumor
- e) Malformative tumor

24. Microscopic rosette formation is characteristic feature of:

- a) Astrocytoma
- b) Oligodendroglioma
- c) Medulloblastoma
- d) Meningioma
- e) Schwannoma

25. Mode of infection in poliomyelitis is:

- a) Ingestion of contaminated food or drink
- b) Droplet infection
- c) Blood spread from septic focus
- d) Direct spread from air sinus

26. Mycotic cerebral aneurysm is due to:

- a) Congenital weakness of the wall of cerebral vessels
- b) Septic emboli from subacute bacterial endocarditis
- c) Atherosclerosis of cerebral vessels
- d) Increased intracranial tension

27. Hypertensive patient are at high risk of:

- a) Extradural hemorrhage
- b) Subarachnoid hemorrhage
- c) Subdural hemorrhage
- d) Intracerebral hemorrhage

28. Congenital cerebral aneurysm affects:

- a) Blood vessels of circle of wills
- b) Cerebral arteries
- c) Meningeal arteries
- d) Internal carotid artery

29. Multiple sclerosis is:

- a) Congenital disease
- b) Inflammatory disease
- c) Degenerative disease
- d) Demyelinating disease
- e) Metabolic disease

30. Negri bodies are:

- a) Inflamed granulation tissue
- b) Aggregates of organizing fibrin
- c) Epithelioid granulomas
- d) Foreign body granulomas
- e) Intracytoplasmic inclusions

31. CSF in acute septic meningitis does not show:

- a) Increased amount
- b) Increased protein content
- c) Increased sugar content
- d) Increased PNL cells
- e) Organisms

32. Astrocytoma is not:

- a) A glial tumor
- b) The commonest primary brain tumor in adults
- c) Always in cerebral hemispheres
- d) Classified into grades according to degree of nuclear atypia

33. Muscle paralysis in case of poliomyelitis is due to:

- a) Destruction of muscles fibers by toxins of the organisms.
- b) Inflammation of muscle fibers (myositis)
- c) Inflammation of nerves supplying the affected muscles (peripheral neuropathy)
- d) Degenerative and demyelination of motor nerves

34. A male patient 40 years old, presented with hemiplegia and deafness. Radiologic examination shows a tumor at the cerebellopontine angle. Biopsy from this tumor shows a neurogenic

tumor formed of hypercellular and hypocellular areas. The most possible diagnosis is:

- a) Neuroblastoma
- b) Schwannoma
- c) Ganglioneuroma
- d) Ganglioneuroblastoma
- e) Neurofibroma

Cases

1) A 58-year-old hypertensive patient presents with sudden onset of hemiplegia, followed by symptoms of increased intracranial tension (headache & vomiting). A CT scan shows extensive intracerebral haemorrhage in the region of basal ganglia.

- What is the most likely cause of this cerebral haemorrhage?
- What are expected cause and complications in this case?
- What is the direct cause of death?

2) A 5-year-old boy presents with a mid-line cerebellar tumor. Sections prepared from the excised tumor reveal extremely cellular neoplasm, formed of anaplastic small cells.

- What is the most likely diagnosis?
- What is the most helpful microscopic feature?
- What is the cell of origin of this neoplasm?
- Mention another cerebellar tumor occurring in the same age, But with more better prognosis.

3) A 68-year-old man suffers from dementia for a long period. He died in a car accident. During autopsy investigations, silver stain was performed on sections of the frontal, parietal and temporal cortex. It reveals intraneuronal inclusions.

- What is the most likely diagnosis?
- What do you call those intraneuronal inclusions? Describe it
- What are other expected microscopic findings in this case?
- Describe the naked-eye appearance of the brain in this patient.

4) A 33-year-old male presents with seizures (neurological symptoms). MRI scans show an ill-defined area of infiltrative tumor expanding the frontal lobe. Biopsy of the lesion shows glial tissue, with slightly increased cellularity and mild nuclear pleomorphism. No mitotic activity, no necrosis and no vascular proliferation.

- What is the most likely diagnosis?
- What are the parameters for diagnosing Glioblastoma multiforme?
- Is there grade 1 astrocytoma? Clarify.

5) An 18-year-old male presents with a well-circumscribed mass involving the 4 ventricle.

- What is the most likely diagnosis?
- Describe the light microscopic features in sections prepared from the tumor
- What are the known variants of this tumor? Describe their gross and microscopic features.
- Enumerate tumors (anywhere) which show rosettes microscopically.

6) A 42-year-old male, with AIDS (HIV-1) develops neurologic symptoms before he dies. Autopsy investigations reveal mild cerebral atrophy without focal lesion. Histologically, foci of multinucleated giant cells are seen, with macrophages and lymphocytes involving the white matter.

- What is the most likely diagnosis?
- What are the other possible effects of HIV-1 on the CNS?
- What is the most common AIDS related neoplasm that may involve CNS?

7) A 9-year-old girl is evaluated for headaches and ataxia (clumsiness with walking) over the last 2 months. A CT scan reveals a midline partially cystic cerebellar mass. Microscopic examination shows elongated bipolar astrocytes with fibrillar processes and Rosenthal fibers.

- What is the most likely diagnosis?
- What are the most common types of primary CNS tumors in children and in adults?
- Mention the microscopic grading for the commonest glial tumor in adults.